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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,994	02/15/2002	Usha Kasid	219604	9186

23460 7590 03/02/2005

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EXAMINER	
ZARA, JANE J	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

4C

Office Action Summary	Application No.	Applicant(s)	
	10/075,994	KASID ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 12-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 12-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 10-12-04.

Claims 1-9, 12-23 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claims 1-9, 12-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for enhanced delivery of any oligonucleotide to target cells in vitro comprising the administration of an oligonucleotide (of 40 nucleobases or less) encapsulated in cationic liposomes consisting of the cationic lipid, phosphatidylcholine and cholesterol and for the chemosensitization of tumor tissue in vivo comprising the co-administration of SEQ ID NO: 1 encapsulated in cationic liposomes consisting of a cationic lipid, phosphatidylcholine and cholesterol in combination with mitoxantrone, cisplatin, epirubicin or Gemzar, does not reasonably provide enablement for the chemosensitization of tumor tissue comprising the administration of any oligonucleotide that specifically targets Raf and optionally further comprising the administration of any chemotherapeutic agent. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the same reasons of record set forth in the Office action mailed 7-13-04.

Applicant's arguments filed 10-12-04 have been fully considered but they are not persuasive. Applicants argue that enablement has been provided for the scope comprising a method of chemosensitizing tumor tissue to any chemotherapeutic agent comprising the administration of any antisense oligonucleotide specifically targeting raf, and which is encapsulated in cationic liposomes consisting of a cationic lipid, phosphatidylcholine and cholesterol. The specification teaches enhanced chemosensitization of human prostate cells in an appropriate animal model comprising the co-administration of the antisense oligonucleotide of SEQ ID NO: 1 encapsulated in cationic liposomes consisting of a cationic lipid, phosphatidylcholine and cholesterol, in combination with the administration of the chemotherapeutic agent mitoxantrone, cisplatin, epirubicin or Gemzar, whereby sensitization of the corresponding and co-administered chemotherapeutic agent is observed. But this is not representative of tumor chemosensitization to any chemotherapeutic agent (of which very broad genera are generically mentioned) following the administration of any oligonucleotide that targets raf. Encapsulated antisense of SEQ ID NO: 1 has been shown to be effective in targeting and inhibiting the expression of raf in vivo. And encapsulated SEQ ID NO: 1 has been shown to be effective in chemosensitizing tumors to a chemotherapeutic agent that was co-administered with it, and selected from mitoxantrone, cisplatin, epirubicin or Gemzar. The examples of enhanced chemosensitization upon co-

administration of SEQ ID No: 1 are not representative of the ability of any antisense to provide such treatment effects in vivo, nor are they representative of the ability to sensitize tumor cells to a different agent than the one co-administered with antisense of SEQ ID NO: 1, nor are they representative of the ability to sensitize tumor cells by previous or post administration of SEQ ID NO: 1 or any other antisense. Efficacy involving the various scenarios listed directly above, and which are broadly claimed in the instant invention, require undue experimentation beyond that taught in the instant specification. The chemosensitization upon co-administration of SEQ ID NO: 1 and cisplatin, for instance, is not correlative or representative of the ability to achieve sensitization to another chemotherapeutic agent using a different and distinct mechanism of action (e.g. using a peptide, antibody, or natural product as broadly claimed and defined in the instant specification). Furthermore, the ability of SEQ ID NO: 1 to target and inhibit the expression of raf in vitro or in vivo is not representative of the ability of other antisense oligonucleotides targeting raf to inhibit its expression in vivo, and further whereby provide chemosensitization to any broadly claimed chemotherapeutic agent in an organism. It would take undue experimentation beyond that provided in the instant disclosure to identify additional antisense oligonucleotides that provide for in vivo target gene inhibition and further provide for the treatment effects claimed. For these reasons, the scope of enablement rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JZ
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